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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,334	05/25/2005	Boris Linard	258087US0XPCT	8821

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OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
REDDIG, PETER J	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
08/28/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/506,334	LINARD ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *4-25 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 26* is/are rejected.

7)☒ Claim(s) *26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 September 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/2/04 3/14/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Election filed 6/13/2007 in response to the Office Action of March 13, 2007 is acknowledged and has been entered. New claims 25-27 have been added.

Applicant's election with traverse of Group I, claims 1-3, drawn to a medicinal product for antitumor immunotherapy comprising one peptide, SEQ ID NO: 1 is acknowledged.

The traversal is on the ground(s)the Examiner has not provided any indication that the contents of the claims were interpreted in **light of** the description in making the assertion of a lack of unity.

Applicants' arguments have been considered, but have not been found persuasive. Although the claims are interpreted in light of the description, the limitations of the specification are not read into the claims. Given that Thomson et al. teach a peptide that comprises a claimed version of SEQ ID NO: 1, the product of the prior art comprises the same product as claimed in the instant invention, that is, a peptide that comprises a claimed version of SEQ ID NO: 1, thus the claimed product is anticipated because the product will inherently be capable of inducing a cytotoxic response directed against the Melan-A antigen. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Although the reference does not specifically state that the peptide was capable of inducing a cytotoxic response directed against the Melan-A antigen, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed method is different from those taught by the

prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA). The preamble of a medicinal product for antitumor immunotherapy in an HLA-B35 patient is merely suggestive of an intended use and is not given weight for purposes of comparing the claims with the prior art. The claims read on the active ingredients per se, *i.e.* the claimed peptides. Thus, the finding of lack of unity in view of Thomson et al. is deemed appropriate.

Applicants argue that the Examiner has not provided sufficient reasons and/or examples to support the assertion that the combination/subcombinations are distinct.

Applicants' arguments have been considered, but have not been found persuasive because reasons have been given in the previous Office action that each subcombination is useful for screening for different variables and different markers and treatment of different disease, which is not simply a conclusion as argued by Applicants. For instance, the different combinations of peptides can be used to elicit immune responses to distinct combinations of antigens.

For the reasons set forth above and previously, the restriction requirement is deemed to be proper and is therefore made FINAL.

2. Claims 1-27 are pending.

3. Claims 4-25 and 27 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

4. In view of the prior art SEQ ID NO: 8 will be rejoined for examination. Additionally, given that SEQ ID NO: 10 is one form of SEQ ID NO: 1 SEQ ID NO: 10 will be rejoined for examination.

5. Claims 1-3 and 26 are currently under consideration as drawn to SEQ ID NO: 1, SEQ ID NO: 8, and SEQ ID NO: 10.

Priority

6. It is noted that examiner has established a priority date for the instant application, 10/520,224, of 4 March 2003 because the priority of the instantly claimed invention is based on the French Application 02/02703, which has not been translated and the Examiner is unable to determine the information in the document.

If applicant disagrees with any rejection set forth in this action based on Examiner's establishment of a priority date, 4 March 2003 for the instantly claimed application serial number 10/520,224, Applicant is invited to submit a proper translation of the priority document and to point to page and line where support can be found establishing an earlier priority date. If Applicants choose to file a translation, then the translation must be filed together with a statement that the translation of the certified copy is accurate, see MPEP 201.15.

Drawings

7. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: The brief description to figure 3 does not contain a description of all of the line symbols used in figure 3. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet

submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

8. The disclosure is objected to because of the following informalities: There is not a separate brief description of the drawings section and there is no clear delineation of the sections of the specification.

Appropriate correction is required.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).

(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Content of Specification

(a) Title of the Invention: See 37 CFR 1.72(a) and MPEP § 606. The title of the invention should be placed at the top of the first page of the specification unless the title is provided in an application data sheet. The title of the invention should be brief but technically accurate and descriptive, preferably from two to seven words may not contain more than 500 characters.

(b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.

(d) The Names Of The Parties To A Joint Research Agreement: See 37 CFR 1.71(g).

(e) Incorporation-By-Reference Of Material Submitted On a Compact Disc: The specification is required to include an incorporation-by-reference of electronic documents that are to become part of the permanent United States Patent and Trademark Office records in the file of a patent application. See 37 CFR 1.52(e) and MPEP § 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text were permitted as electronic documents on compact discs beginning on September 8, 2000.

(f) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(g) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(h) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

(i) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(j) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet or electronic page (37 CFR 1.52(b)(3)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP § 608.01(i)-(p).

(k) Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims. In an international application which has entered the national stage (37 CFR 1.491(b)), the applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).

(l) Sequence Listing, See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02.

9. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, on p. 12, line 14. Removal of the "http://" will disable the hyperlink and obviate this objection, See MPEP § 608.01.

Claim Objections

10. Claim 26 is objected to because of the following informalities: A word appears to be missing between "at least" and "immunogenic". Appropriate correction is required.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 2 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Speiser et al. (European J. of Immunology, 15 February 2002, 32:731-741).

The claims are drawn to

1. A medicinal product for antitumor immunotherapy in an HLA-B35 patient comprising at least one immunogenic peptide representing a T epitope presented by MHC I, wherein the peptide is a peptide comprising the sequence $EX_1AGIGILX_2$ (SEQ ID NO: 1) in which X_1 represents A or P, and X_2 represents T or Y, capable of inducing a cytotoxic response directed against the Melan-A antigen.

2. The medicinal product of claim 1, wherein said peptide is selected from the group consisting of: a) a peptide of sequence selected from the group consisting of EAAGIGILTV (SEQ ID NO: 8) and EAAGIGILY (SEQ ID NO:10).

26. A medicinal product for antitumor immunotherapy in an HLA-B35 patient comprising at least one immunogenic peptide representing a T epitope presented by MHC I, wherein the peptide is a peptide comprising the sequence $EX_1AGIGILX_2$ (SEQ ID NO: 1) in which X_1 represents A or P, and X_2 represents T or Y, capable of inducing a cytotoxic response directed against the Melan-A antigen.

Speiser et al. teaches that the injection of Melan-A/MART-1_{26-35} peptide EAAGIGILTV into an advance stage melanoma patient, LAU337, increased the frequency of antigen specific, activated T cells, see Materials, and Methods, Fig. 3 and 4 and p. 733, 2nd col.-734. Speiser et al. teach that patient LAU337, who was treated with the Melan-A/MART-1_{26-35} peptide EAAGIGILTV, experienced regressions of multiple lesions, see p. 737, left col.

Given that Speiser et al. teach a peptide that comprises a claimed version of SEQ ID NO: 1, which is identical to SEQ ID NO: 8 and SEQ ID NO: 8 meets the requirements of the consensus sequence of SEQ ID NO: 1, and a patient treated with the peptide experienced regression of lesions, the product of the prior art comprises the same product as claimed in the instant invention, that is, a peptide that comprises a claimed version of SEQ ID NO: 1, thus the claimed product is anticipated because the product will inherently be capable of inducing a cytotoxic response directed against the Melan-A antigen. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Although the reference does not specifically state that the peptide was capable of inducing a cytotoxic response directed against the Melan-A antigen, the claimed product appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and

functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed method is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over by Speiser et al. (European J. of Immunology, 15 February 2002, 32:731-741) as applied to claims 1, 2, and 26 above, further in view of Falk et al. (Immunogenetics 1993, 38: 161-162), and further in view of Schultz et al. (Tissue Antigens 2001. 57:103-109).

Claim 3 is drawn to an immunogenic peptide representing a T epitope presented by MHC I, wherein the peptide is EAAGIGILY (SEQ ID NO:10).

Speiser et al. teach as set forth above.

Speiser et al. do not teach EAAGIGILY.

Falk et al. teach that each MHC allelic product has its individual peptide specificity, summarized as a peptide motif that is characterized by the position and occupancy of anchor residues whose side chains protrude into complementary pockets inside the peptide accommodating groove of the respective MHC molecules. Falk et al. teach that many class I molecules show a preferential peptide length see p. 161, first col. Falk et al. teach that the MHC-B35 specific motif is predominantly 9 amino acids with a conserved, anchored tyrosine or hydrophobic residue at position 9, see p.161, 2nd col. Falk et al. also teach that alanine is found naturally at the position 2 anchor site of HLA-B35 interacting peptides, see Table 1

Schultz et al. teach that HLA-B35 molecules are expressed by 20% of Caucasians, p. 108, left col.

Thus, it would be *prime facia* obvious to one of skill in the art at the time the invention was made to modify the peptide of Speiser et al. by reducing the peptide to the preferred HLA-B35 length and changing position 9 to a tyrosine given that tyrosine is that natural anchor residue for HLA-B35 and 9 amino acids is the preferred length. Given that Speiser et al. teaches that

EAAGIGILTV was able to initiate regression of melanoma and given that the peptide already contains an alanine at the position 2 anchor site, which is taught by Falk et al. to be a naturally occurring amino acid at that position, one would have been motivated with a reasonable expectation of success to modify the peptide to a natural HLA-B35 motif with a tyrosine at position 9 to increase the interaction of the peptide with HLA-B35 and increase the immunogenicity of the peptide. Furthermore, given that HLA-B35 is present in significant percentage of individuals susceptible to melanoma, one would had been motivated to target the HLA-B35 MHC molecule to be able to treat a large population with a single agent.

13. No claims allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

Peter J. Reddig
Examiner
Art Unit 1642

PJR